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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,365	07/03/2003	Fred C. Christians	3299.2	4821

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EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/613,365	CHRISTIANS ET AL.	
	Examiner	Art Unit	
	Amanda M. Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 56-68 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 56-68 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 16 January 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

The Preliminary Amendment received on 7/3/2003 is acknowledged. During the interview on 11/2/2005 the Applicant stated that Claims 1-55 and 69 are cancelled. Claims 56-68 are pending and will be examined in this Office Action.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60162739 filed October 10,1999 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for the presently claimed method for labeling a polynucleotide compromising: contacting said polynucleotide with PEO-iodoacetyl conjugated to a signal moiety under conditions such that the PEO-iodoacetyl will attach to said nucleotide. Also it fails to provide adequate support or enablement in the manner provided by the

first paragraph of 35 U.S.C. 112 for the presently claimed method for labeling a polynucleotide compromising: contacting said polynucleotide with a reactive thiol group to form a thiolated polynucleotide; contacting said thiolated polynucleotide with a signal moiety capable of reacting with said thiolated polynucleotide under appropriate conditions such that said signal moiety is attached to said polynucleotide.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on July 3, 2003 and June 2, 2004 have been received. The references listed in the IDS have been reviewed as indicated on the 1449, and a copy is attached herein.

Specification

a. The amendment filed July 3, 2003 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is as follows: throughout the specification, grams have been changed to micro grams and liters have been changed to micro liters.

Applicant is required to either cancel the new matter in the reply to this Office Action or change this application to a Continuation in Part.

b. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: A novel method for labeling polynucleotides.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more Claims particularly pointing out and distinctly Claiming the subject matter which the applicant regards as his invention.

Claims 56-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 64 is indefinite for the recitation "wherein said step of creating a thiol group comprises" because the recitation lacks proper antecedent basis in Claim 63.

Claims 56-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that the goal of the method and the final step do not agree. Claims 57-62 are dependent upon Claim 56, which is a method of labeling a polynucleotide. The steps listed in the method do not result in a labeled nucleotide. Therefore, it is unclear if the steps listed can achieve the goal of the method.

Claims 63-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that the goal of the method and the final step do not agree. Claims 64-68 are dependent upon Claim 63, which is a method of labeling a polynucleotide. The steps listed in the method do not result in a labeled nucleotide. Therefore, it is unclear if the steps listed can achieve the goal of the method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 63, 64, and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Szostak et al (U.S. Patent 5688670).

Regarding Claim 63, Szostak et al teach a method for labeling a polynucleotide by contacting the polynucleotide with a reactive thiol group to form a thiolated polynucleotide that binds to a signal moiety (Column 15, lines 43-48).

Regarding Claim 64, Szostak et all teach the method of claim 63 wherein said step of creating a thiol group comprises contacting said polynucleotide with a ATP-gamma-S and a kinase (Column 13 lines 26-28).

Regarding Claim 67, Szostak et all teach the method of Claim 63 wherein said polynucleotide is an RNA (Column 15, line 25).

Claims 56,57,61, 63, 65, and 67 are rejected under 35 U.S.C. 102(e) as being anticipated by Laayoun et al (U.S. Patent No. 6489114, filed December 18, 2000 which claims priority to Provisional Application 60,172,135 filed December 17, 1999).

The applied reference has two common inventors with the instant application (Duc Do and Charles G. Miyada). Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Regarding Claim 56, Laayoun et al teach a method for labeling a polynucleotide with PEO-iodoacetyl attached to a signal moiety (i.e. biotin, Provisional Application Page 17, lines 16- 26).

Regarding Claim 57, Laayoun et al teach the method of Claim 56 wherein said polynucleotide comprises a thiol group (i.e. oligoribonucleotide 3'-monothiophosphate, Provisional application Page 17, line 14).

Regarding Claim 61, Laayoun et al teach the method of Claim 56 wherein said polynucleotide is an RNA (i.e. oligoribonucleotide 3'-monothiophosphate, Provisional application Page 17, line 14).

Regarding Claim 63, Laayoun et al teach a method for labeling a polynucleotide by contacting the polynucleotide with a reactive thiol group to form a thiolated polynucleotide that binds to a signal moiety (Provisional Application Page 17, lines 9-26).

Regarding Claim 65, Laayoun et al teach the method of Claim 63 wherein said signal moiety is a biotin (Provisional application Page 17, line 26).

Regarding Claim 67, Laayoun et al teach the method of Claim 63 wherein said polynucleotide is an RNA (i.e. oligoribonucleotide 3'-monothiophosphate, Provisional application Page 17, line 14).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 56-59, 61, 63,65, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drolet et al (U.S. Patent No. 5,789,163, issued August 4, 1998) in view of Pierce Biotechnology, Inc.

Regarding Claim 56, Drolet et al teach a method for labeling a polynucleotide by contacting the polynucleotide with Iodoacetyl-LC Biotin (Column 11, line 42-43).

Regarding Claim 56, Drolet et al do not teach a method for labeling polynucleotides by contacting the polynucleotides with Iodoacetyl-PEO-Biotin.

Pierce teaches that Iodoacetyl-LC-Biotin and Iodoacetyl-PEO-Biotin are similar reagents for attaching Biotin to modify molecules. Pierce also teaches that Iodoacetyl-LC-Biotin requires organic solvents and is not soluble in water. Iodoacetyl-PEO-Biotin does not require organic solvents and imparts high water solubility and adds solubility to the molecules being modified (Pierce Reference A, Page 1 and Pierce Reference B, Page 1). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the Iodoacetyl-LC-Biotin taught by Drolet to label RNA with Iodoacetyl-PEO-Biotin instead of Iodoacetyl-LC-Biotin. One of ordinary skill in the art would have been motivated to use an Iodoacetyl-PEO-Biotin for the expected benefits of reduced exposure to organic solvents but more importantly the added solubility to the modified molecules.

Regarding Claim 57, Drolet et al teach the method of Claim 56 wherein said polynucleotide comprises a thiol group. The thiol group was added by GDP-beta-S (Column 11, line 36-39).

Regarding Claim 58, Drolet et al teach the method of Claim 57 wherein the said thiol group is at the 5' end. The thiol group was added by GDP-beta-S to the 5' end of the RNA (Column 11, line 36-39).

Regarding Claim 59, Drolet et al teach the method of Claim 58 wherein said signal moiety is a biotin (i.e. Iodoacetyl-LC-Biotin Column 11, line 42-43).

Regarding Claim 61, Drolet et al teach the method of Claim 56 wherein said polynucleotide is a RNA (Column 11, line 42-43).

Regarding Claim 63, Drolet et al teach a method for labeling a polynucleotide by contacting the polynucleotide with a reactive thiol group to form a thiolated polynucleotide that binds to a signal moiety (Column 11, lines 32-42).

Regarding Claim 65, Drolet et al teach the method of Claim 63 wherein said signal moiety is a biotin (i.e. Iodoacetyl-LC-Biotin, Column 11, line 42-43).

Regarding Claim 67, Drolet et al teach the method of Claim 63 wherein said polynucleotide is an RNA (Column 11, line 42-43).

Claims 60, 62, 66, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drolet et al (U.S. Patent No. 5,789,163, issued August 4, 1998) in view of Pierce as applied to Claims 56 and 63 above and further in view of Mattheakis et al (U.S. Patent No. 5,922,545, issued July 13, 1999).

Regarding Claim 60, Drolet et al teach the method of Claim 56 where in the said polynucleotide is an RNA (Column 11, lines 42-43).

Drolet et al do not teach the method of Claim 56 where in the said polynucleotide is an DNA.

However it was well know in the art at the time the invention was made to place a linker between biotin and mRNA or DNA for the purpose of avoiding adverse affects of translational efficiency of the mRNA as taught by Mattheakis et

al (Column 33, lines 6-12). One of ordinary skill in the art would have been motivated to combine the teachings of Drolet, Pierce and Mattheakis and thereby add the Iodoacetyl-PEO-Biotin linker to mRNA and DNA for the expected benefit of avoiding adverse affects of translational efficiency of the mRNA as desired by Mattheakis et al (Column 33, lines 6-12).

Regarding Claim 62, Mattheakis et al teach the method wherein said polynucleotide is a mRNA (Column 33, lines 21-24).

Regarding Claim 66, Mattheakis et al teach the method wherein said polynucleotide is a DNA (Column 32, lines 29-31).

Regarding Claim 68, Mattheaksi et al teach the method wherein said polynucleotide is a mRNA (Column 33, lines 21-24).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 8am-5pm. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634
November 21, 2005

BJ FORMAN, PH.D.
PRIMARY EXAMINER